Department of Biochemistry,
University of Cambridge,
17 December 1957

Dear Dr Lederberg,

Your altogether charming and disarming letter has undone me and I feel it was well worth waiting a year to hear from you. Thank you for your kindness in replying at such length and with such felicitous phrase to my enquiries.

I respond in some haste because a final draft of the proposed letter to Nature has been concocted and is girdling the globe and I would feel the usefulness doubly secure were your name to appear on it along with the others who have agreed to sign. You may notice that I have slightly modified the original wording in the light of your remarks (and others) but do not feel able to crusade at this time for the all-embracing term you desire (and I would favour). Is it not perhaps best to establish first the correct usage for one term and then go on to invent such new terms as are necessary and agreeable ? The disease you mentioned can be chronic or acute but also its effects may be malignant or benign. As you say usage takes precedence over aesthetics but although the existing circumlocutions are far from ideal (osmotically-sensitive spherical forms, etc.) they are simply descriptive and are sufficiently variable (globular for spherical and so on) that they need not become rigidified into forms which are later regretted because they imply too much, too little or something errant. Of all your alternatives I think I like best MALAKOPLAST while HABROCYTE is least euphonious. Since it is a Heraklean task to get two or three people to agree on a definition and since there seems some chance of half a score putting signatures to this note of mine, would it not be well to cry "mirabile dictu" and leave it at that for the time being ?

To turn to your query concerning other lesions in Gram-negative walls. It would seem that four components are involved:
Protein, lipid, polysaccharide (or lipopolysaccharide) and mucopolysaccharide.
The latter contains the D-amino acids, DAP, hexosamines and so on; the polysaccharide, the mannoheptose and other sugars. Already I have suggested to Toennessand Shockman that with their Strp. faecalis 9790 restriction of D-amino acids should lead to similar effects to lysine deficiency and that it might be possible to derive protoplasts thus. The exact experiments I had in mind have not be done but related ones showed lysis when D-alanine became limiting as predicted but this was followed by a fresh wave of growth - perhaps due to some synthesis of B6. However, it seems to me that all these approaches - muramic acid, D-amino acids, glucoasmine, DAP etc. are all aimed at the same component - the mucopolysaccharide. What is needed is additional deprivation. How about ethanolamine ? Or a double mutant DAP and ethanolamine ? My thinking starts from a belief that it is likely that there is lipoprotein in both cell wall and cytoplasmic membrane and that therefore chemical methods are probably not adequate to distinguish the two. But biochemical methods might - it is possible that the lipid is

also glycogen, basically, phage entry.

different in the two structures - for instance we have recently analysed the protoplast membrane of M. lysodeikticus after removal of the cell wall with lysozyme. The wall contains four amino acids and glucose and a lot of glucoasmine and muramic acid. The protoplast membrane (cytoplasmic membrane ?) is 50% protein containing all the usual amino acids, 28% lipid (more than 80% phosphlipid but not containing any N - i.e. no ethanolamine, serine, choline etc.) and is probably polyphosphatidic acid) and 15 - 20% carbohydrate - largely mannose probably with next to no glucose and very little if any amino sugar. Weibull has analysed the lipids of B. megaterium and again finds most of the total lipid is polyphosphatidic acid. Perhaps the lecithin type phosphatides occur in Gram-negatives walls and not membranes so that ethanolamine deprivation would impair wall but not membrane. This kind of approach I think might be fruitful.

I finished a week or two ago my chapter on Bacterial Protoplasts for Gunsalus and Stanier's book on "The Bacteria" and wish I could have seen your paper before writing it. However, I gambled on the Gram negatives being "protoplasts" rather than protoplasts stricto sensu and it seems that it came off.

I shall write again later if I may and in the meantime may I ask that you consider whether or not you feel able to sign this note to Nature ?

All good wishes,

Yours sincerely,

Kenneth McQuillen.

P. S. I shall send you under separate cover the MS of a paper on the chemistry of the protoplast membrane in M. lysodeikticus, a note I wrote for Lancet, the MS of a symposium contribution on Bacterial Lysis resulting from metabolic disturbance. I have also a copy of my chapter on protoplasts which you are welcome to see if you would so wish. It is bulky and has to go to one or two other people but please let me know if it would be of any interest to you.

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